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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/348,469	07/07/1999	AUSTIN GERARD SMITH	06999.0001-01000	5288
23380	7590	08/11/2004	EXAMINER	
TUCKER, ELLIS & WEST LLP 1150 HUNTINGTON BUILDING 925 EUCLID AVENUE CLEVELAND, OH 44115-1475			ANGELL, JON E	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/348,469	SMITH ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-34,41,42,54,55 and 61-74 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-34,41,42,54,55 and 61-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 July 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 08/537,767.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/03 & 6/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Action is in response to the communication filed on 5/3/04. The amendment has been entered. Claims 22-34, 41, 42, 54, 55 and 61-74 are pending in the application and are addressed herein.

Claims 30, 31, 54, 55 and 61-72 were previously withdrawn from consideration pursuant to 37 CFR 1.142(b) (See Office Action dated 10/30/03). However, upon further consideration, in light of the fact that the previously examined claims encompassed mouse embryonic stem cells as well as descendants of said mouse embryonic stem cells, previously withdrawn claims 30, 31, 54, 55 and 61-72 are rejoined with the currently pending claims, and the restriction is withdrawn.

All pending claims are examined herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/24/04 and 7/9/03 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the information disclosure statements.

Terminal Disclaimer

The terminal disclaimer filed on 5/3/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Patent No. 6,150,169 has been reviewed and is accepted. The terminal disclaimer has been recorded. Since the terminal disclaimer has been accepted, the rejection of claims

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under the judicially created doctrine of obvious-type double patenting has been withdrawn.

Specification

The disclosure is objected to because of the following reasons: the specification discloses sequences which require the appropriate sequence identifiers (SEQ ID NO.). For example, see pages 27 and 28 of the specification. Without the appropriate sequence identifiers (SEQ ID NO.), the application is not in sequence compliance. It appears that the sequences disclosed in the specification are sequences that are listed in the Paper Sequence listing, which does have appropriate SEQ ID NO. assigned to each sequence. Therefore, it appears that applicants merely need to amend the specification such that the appropriate SEQ ID NO. is listed with each sequence in the specification.

Appropriate correction is required.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the residence and post office address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Specifically, the post office address of Richard Lathe is not provided.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 26-31, 41, 61 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite for the following reasons:

Claim 22 is drawn to a method for inserting a heterologous gene coding sequence into an endogenous gene in a mouse embryonic stem cell comprising the step of transforming the mouse embryonic stem cell with a random gene trap vector comprising a DNA construct, wherein the heterologous gene coding sequence lacks a promoter, and (ii) comprises the sequence: 5' X-A-P-B-Q-C-Y 3' in which X and Y are substantially homologous with a host gene locus... wherein Q is the heterologous gene sequence, including a translation start codon... etc.

First, the method comprises the step of transforming the mouse embryonic stem cell with a random gene trap vector comprising sequences X and Y, which are substantially homologous with a host gene locus. The phrase “random gene trap vector” renders the instant claims indefinite because the gene trap vector comprises sequences substantially homologous with a host gene locus, indicating that the vector integrates into a target gene by homologous recombination, not by random integration. Therefore, the

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gene trap vector is not a “random” gene trap vector. Furthermore, claim 23 specifically recites that the heterologous gene coding sequence is randomly inserted into an endogenous gene. Again, since the vector comprises sequences substantially homologous with a host gene locus, the heterologous gene coding sequence integrates by homologous recombination and not randomly. It is suggested that the phrase “random gene trap vector” should be changed to “gene trap vector” (claim 22) and the word “randomly” should be deleted from claim 23.

Second, the claim is indefinite because the phrase, “the heterologous gene coding sequence... comprising the sequence X-A-P-B-Q-C-Y” wherein Q is the heterologous gene sequence...” indicates that the heterologous gene coding sequence comprises itself (i.e. element Q, which is “the heterologous gene sequence”). It is unclear how the heterologous gene coding sequence can comprise the heterologous gene sequence. The claim should be amended, and a suggestion is provided below.

Third, the claim encompasses “a gene trap vector comprising a DNA construct, wherein the heterologous gene coding sequence lacks a promoter, and (ii) comprises the sequence...” Here, it appears that the claim encompasses multiple elements, however only element (ii) is clearly indicated, not element (i). Therefore the claim is indefinite because it is unclear if element (i) is missing from the claim.

Fourth, the phrase “the heterologous gene sequence” in line 11 renders the claim indefinite because it is unclear what “heterologous gene sequence” the phrase is referring to. The claim should be amended and a suggestion is provided below.

Overall, the claim is very confusing. There are multiple problems (indicated above) which render claim 22 (and dependent claims: 23, 24, 26-31, 41, 61 and 62)

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indefinite. Applicants are asked to consider the following claim which would not be considered indefinite:

A method of inserting a heterologous gene coding sequence into an endogenous gene in a mouse embryonic stem cell such that the heterologous gene coding sequence expresses a gene of interest in said mouse embryonic stem cell, wherein said method comprises transforming the mouse embryonic stem cell with a gene trap vector comprising the heterologous gene coding sequence: 5' X-A-P-B-Q-C-Y 3' wherein:

X and Y are substantially homologous with separate sequences of the endogenous gene, and are of sufficient length to undergo homologous recombination with the endogenous gene so as to insert the A-P-B-Q-C-Y elements into the host cell's genome;

P is an internal ribosome entry site (IRES);

Q is the gene of interest;

A, B and C are, optionally, separate linker sequences;

a polyadenylation site is located 3' (downstream) of Q;

a splice acceptor site is located 5' (upstream) of P;

and wherein the heterologous gene coding sequence lacks a promoter element.

Claims 32-34, 42, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant rejection is similar to the rejection of claims 22-24, 26-31, 41, 61 and 62 above. Claims 32-34 and 42, however, are drawn to a DNA construct for randomly inserting a heterologous gene sequence into a mouse cell genome wherein said

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heterologous gene sequence lacks a promoter and comprises the sequence 5' X-A-P-B-Q-C-Y 3' as indicated above. Claims 73 and 74 are drawn to A DNA construct for inserting a heterologous gene coding sequence into a target gene in a eukaryotic host cell genome wherein the comprises the elements 5' X-A-P-B-Q-C-Y 3' as indicated above.

Similar to the rejection above, the claims 32-34 and 42 encompasses a random gene trap vector comprising sequences X and Y, which are substantially homologous with a host gene locus. The phrase "random gene trap vector" renders the instant claims indefinite because the gene trap vector comprises sequences substantially homologous with a host gene locus, indicating that the vector integrates into a target gene by homologous recombination, not by random integration. Therefore, the gene trap vector is not a "random" gene trap vector. Amending the claim to "a gene trap vector" would obviate this reason for rejection.

Second, claims 32-34, 42, 73 and 74 are indefinite because the phrase, "said heterologous gene sequence lacking a promoter and comprising the sequence X-A-P-B-Q-C-Y" wherein "Q is the heterologous gene sequence..." indicates that the heterologous gene sequence comprises itself. It is unclear how the heterologous gene sequence can comprise itself. The claim should be amended, and a suggestion is provided below.

Overall, the claim is very confusing. There are multiple problems (indicated above) which render claim 32 (and dependent claims: 33, 34 and 42) as well as claims 73 and 74 indefinite. Applicants are asked to consider the following two claims which would not be considered indefinite:

(Suggested substitution for claim 32): A DNA construct for inserting a heterologous gene sequence into a mouse cell genome wherein said DNA construct

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comprises the heterologous gene sequence which lacks a promoter element and which comprises the sequence: 5' X-A-P-B-Q-C-Y 3' wherein:

X and Y are substantially homologous with separate sequences of an endogenous gene, and are of sufficient length to undergo homologous recombination with the endogenous gene so as to insert the A-P-B-Q-C-Y elements into the mouse cell's genome;

P is an internal ribosome entry site (IRES);

Q is a gene of interest;

A, B and C are, separately, optional linker sequences;

a polyadenylation site is located 3' (downstream) of Q; and,

a splice acceptor site is located 5' (upstream) of P.

(Suggested substitution for claim 73): A DNA construct for inserting a heterologous gene sequence into a target gene in the genome of a eukaryotic cell, wherein said DNA construct comprises the heterologous gene sequence which comprises the sequence: 5' X-A-P-B-Q-C-Y 3' wherein:

X and Y are substantially homologous with separate sequences of the endogenous gene, and are of sufficient length to undergo homologous recombination with the endogenous gene so as to insert the A-P-B-Q-C-Y elements into the genome of the host cell;

P is an internal ribosome entry site (IRES);

Q is a gene of interest;

A, B and C are, separately, linker sequences or covalent bonds.

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Claims 54, 55 and 63-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because they depend on claims that have been cancelled; therefore, the metes and bounds of the claims cannot be determined. In the interest of compact prosecution, the instant claims are herein interpreted to depend on the closest pending claim. Specifically, claim 54 is interpreted as depending on claim 28, claim 55 then properly depends on claim 54; claim 63 is interpreted as depending on the method of claim 22, claim 64 then properly depends on claim 63; claim 65 is interpreted as depending on the method of claim 22, and claim 66 then properly depends on claim 65.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 54, 55 and 61-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

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Wands states on page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention

The instant claims are drawn to mouse embryonic stem cells, as well as descendants thereof including transgenic animals wherein the cells and animals comprise heterologous gene sequences inserted using the described constructs. Since the only use for the mouse embryonic stem cells contemplated in the specification is for making transgenic animals, the nature of the invention, with respect to the instant claims are transgenic animals made using the claimed gene trap constructs.

The breadth of the claims

It is noted that the claims are drawn to mouse embryonic stem (ES) cells as well as transgenic animals wherein the cells and the animals comprise a heterologous gene sequence that includes a gene of interest such that the gene of interest is expressed in the cell or animal. The claims, however, do not limit the gene of interest (which is expressed in the cells and transgenic animals) to any specific gene. As such, the claims are enormously broad and encompass genetically modified mouse ES cells as well as transgenic animals wherein the modified mouse ES cells and transgenic animals express *any* gene of interest wherein the gene of interest is inserted using the claimed sequence. Therefore, the claims are drawn to a genus of mouse ES cells and transgenic animals wherein the genus encompasses thousands, if not millions of different species considering

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every possible gene of interest that could be inserted into an ES cell using the claimed method.

Furthermore, the claims do not indicate that the transgenic animals have any specific phenotype.

The unpredictability of the art and the state of the prior art

As indicated above, the claims are very broad and encompass mouse ES cells, as well as transgenic animals, wherein the cells/animals have been genetically modified such that the cells/animals express a gene of interest wherein the gene of interest is under the control of an IRES element. The gene of interest could be any gene of interest. Furthermore, the claims do not indicate the transgenic animals have any specific phenotype. Therefore, the specification fails to provide an enabling disclosure for the preparation of the claimed transgenic mice exhibiting an appropriate phenotype. Because the specification discloses no phenotype for the transgenic mice, undue experimentation would have been required for one of skill in the art to make and/or use the claimed invention. To this end, the specification does not provide guidance for any particular phenotype for the claimed transgenic mice, other than the anticipated expression of the transgene.

Note that the mere capability to perform gene transfer in a mouse is not enabling because a desired phenotype cannot be predictably achieved by simply introducing transgene constructs of the types recited in the claims. While gene transfer techniques are well developed for a number of species, and in particular, the mouse, methods for achieving the desired level of transgene expression in appropriate tissues are less well established. The introduction of DNA into the mammalian genome can ordinarily be

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achieved most reliably by microinjection or retrovirus-mediated gene transfer. However, the state of the art for transgenics is unpredictable because the method of gene transfer typically relies on random integration of the transgene construct. Insertional inactivation of endogenous genes and position effects [see Ryan *et al.*, **Sem. Neph.** 22:154-160, 2002] can dramatically influence the phenotype of the resultant transgenic animal. Ryan *et al.* state that methods such as pronuclear injection or gene targeting by homologous recombination are still limited by several unpredictabilities, including differences in transgene copy number and position of integration into the genome. Furthermore, Ryan *et al.* states, "The location of integration can have dramatic effects on the expression of a transgene. Called the position effect, transcriptional regulatory sequences at or near the insertion site can strongly influence (the) transgene, even impart a new set of instructions." [See p. 155, 2nd column].

Furthermore, expression of the transgene and the effect of transgene expression on the phenotype of the transgenic animal depends upon the particular gene construct used, to an unpredictable extent. This is supported by Holschneider *et al.* [**Int J. Devl. Neuroscience** 18:615-618, 2000] who state that the, "knocking out or insertion of a single gene may result in no phenotypic change. This may be the case, in particular, if there exist gene redundancy mechanisms whose presence may prevent abnormal phenotypes from becoming masked. Conversely, single genes are often essential in a number of different behaviors and physiologic processes. Hence, ablation of an individual gene may prove so drastic as to be lethal, or so widespread as to create an amalgam of phenotypes whose interpretation becomes confounded by the interactions of the various new physiologic changes or behaviors." [See p. 615, col. 1-2]. Holschneider

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et al. discuss various factors that contribute to the resulting phenotype of transgenic mice, including compensatory systems which may be activated to mask the resulting phenotype, these compensatory changes may be due to the differential expression of another gene, which may be regulated by the downstream product of the ablated gene, as well as the variability in phenotypic characterization due to particular mouse strains [see p. 616, 1st column].

Given that specific phenotypic alterations cannot be predictably achieved by merely transferring a gene of interest into an animal, specific guidance must be provided to enable the instant invention. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.

Working Examples and Guidance in the Specification

It is acknowledged that the specification discloses three specific working examples wherein a DNA construct comprising a heterologous gene coding sequence is made and used to insert the heterologous gene coding sequence into a animal cell, including a mouse embryonic stem cell as well as an example describing how to make a transgenic animal using the disclosed products and methods. However, as indicated above, the only contemplated use for the stem calls made using the construct is for making transgenic animals (i.e., transgenic mice). As such, the disclosed examples do not correlate to the instant claims because the only contemplated use for the stem cells comprising the heterologous gene coding sequence is for making transgenic mice—which the art recognizes as an unpredictable endeavor, as indicated above. Furthermore, it is respectfully pointed out that the specification does not provide any specific working

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examples wherein a specific transgenic mouse having a specific transgene insertion and exhibiting a specific phenotype has been made. The specification does provide guidance for using the gene trap vector for facilitating integration of a heterologous gene sequence into the genome of cells, including mouse ES cells. However, considering the problems recognized in the art, making a transgenic mouse having a specific desired phenotype is not considered routine experimentation. The guidance provided to make the claimed transgenic animals is not sufficient to overcome the problems recognized in the art, described herein.

Quantity of Experimentation

As previously mentioned, the claims are very broad and encompass transgenic mice that have a heterologous gene sequence inserted into their genome. The claims do not specifically indicate which gene of interest is expressed in the transgenic animals, nor does the disclosure indicate any specific phenotype for the transgenic mice.

Considering the problems recognized in the art, additional experimentation would be required in order for one of skill in the art to be able to make and use the claimed invention to its full scope.

Level of the skill in the art

Considering the level of difficulty with respect to biotechnology in general and, specifically, with respect to the art of making transgenic animals, the level of the skill required to make and use the claimed invention is deemed to be high.

Conclusion

Considering the breadth of the claims, the art recognized problems associated with making transgenic animals, the lack of working examples and guidance, and the

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high degree of skill required, it is concluded that the amount of additional experimentation required to perform the broadly claimed invention is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-31, 54, 55 and 61-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (MCB 1992, cited in IDS filed 6/24/04).

The instant claims are drawn to cells, including mouse embryonic stem cells as well as transgenic mice (and including descendants of the cells/mice), comprising a heterologous gene coding sequence inserted using a gene trap vector that inserts the heterologous gene sequence such that the expression of a gene of interest is controlled by an IRES element.

Kim teaches a mouse embryonic stem cell (which is a cell), as well as descendants of said mouse embryonic stem cell that have inherited the inserted heterologous gene coding sequence (e.g., see abstract, Fig. 3 and Fig. 6). Specifically, Kim teaches the construction of different plasmids wherein the plasmids are used to randomly integrate heterologous gene coding sequences into the genome of mouse embryonic stem cells. The plasmids taught by Kim include an IRES element that regulates the translation of the heterologous gene coding sequence (e.g., see abstract and

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p. 3637). Furthermore, Kim teaches mouse embryonic stem cells that comprise the heterologous gene coding sequence inserted using the indicated plasmid(s). The application of the plasmids to the mouse embryonic stem cells results in mouse embryonic stem cells that have the heterologous gene coding sequence (specifically, β -gal or CAT) under translation control of the IRES element from the integrated plasmid (e.g., see Fig. 3). Since the plasmid has integrated into the host cell's genome, there is no distinguishable difference between the mouse embryonic stem cell taught by Kim and the claimed mouse embryonic stem cell. That is, although the plasmids taught by Kim do not have a splice acceptor site or DNA sequences that are substantially homologous with a host gene locus, once the plasmids integrate into the host cell's genome the resulting mice are indistinguishable from the claimed mice because each has developed from a mouse embryonic stem cell comprising a heterologous gene coding sequence whose translation is regulated by an IRES element.

Furthermore, Kim teaches the mouse embryonic stem cells that express the heterologous gene coding sequence under translational control of the IRES element, can be microinjected into mouse blastocysts (see page 3638, second column). The blastocysts can then be cultured for 2-3 hours and transplanted into pseudopregnant female mice. The developing mice were then recovered at specific stages and stained for beta-galactosidase activity to indicate the presence of the protein encoded by the heterologous gene coding sequence. The results show that beta-galactosidase was present in the transgenic mice, further indicating that the transgenic mice were descendants of the original implanted mouse embryonic stem cell.

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Therefore, the mouse ES cells, embryos and mice taught by Kim meet all of the structural limitations set forth in the instant claims.

Allowable Subject Matter

Claims 22-24, 26, 27, 32-34, 41 and 42 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in herein.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

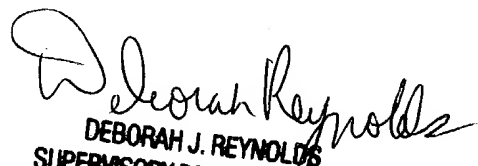
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published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art Unit 1635



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DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600